

# Timing of radiotherapy for men treated with radical prostatectomy

## Radiotherapy for men who have had radical prostatectomy

Men diagnosed with clinically localised prostate cancer are often treated with radical prostatectomy, and have a relatively good prognosis. According to the National Prostate Cancer Audit, more than 7,000 men underwent a radical prostatectomy in England and Wales between April 2017 to March 2018.

Some of these men also receive post-operative radiotherapy. Previous trials have shown a reduced risk of early disease recurrence when patients are given post-operative radiotherapy. However, it is unclear whether having early radiotherapy improves longer-term outcomes compared to a policy of observation with early salvage radiotherapy for PSA failure.

Clinical guidelines offer conflicting advice, with ESMO not recommending post-operative radiotherapy routinely, while the AUA/ASTRO guidelines recommend that patients should be counselled that post-operative radiotherapy reduces the risk of biochemical recurrence, local recurrence and clinical progression.

If men with clinically localised prostate cancer could be spared post-operative radiotherapy unless and until their PSA starts rising (salvage radiotherapy), it could potentially reduce costs to the health system and patients, and avoid unpleasant side-effects. But would this delay in receiving radiotherapy result in worse longer-term outcomes?

This briefing paper is based on the results of the RADICALS-RT trial and ARTISTIC meta-analysis, both of which look at post-operative vs early salvage radiotherapy.

## Key points

- Radical prostatectomy is a standard treatment for locally advanced or localised prostate cancer, with more than 7,000 men undergoing a radical prostatectomy in England and Wales between April 2017 to March 2018.
- Post-operative radiotherapy may be administered to reduce the risk of disease recurrence.
- Alternatively, a strategy of observation with radiotherapy deferred until the PSA levels start to rise (early salvage radiotherapy) may reduce unnecessary treatment and side-effects.
- The RADICALS-RT trial set out to compare outcomes in men with clinically localised prostate cancer randomised to receive either immediate radiotherapy following prostatectomy or early salvage radiotherapy. It showed that immediate radiotherapy did not improve event-free survival compared to early salvage radiotherapy.
- Two similar trials to RADICALS-RT have also recently released results, which have been included in the ARTISTIC meta-analysis.
- With average follow-up of at least five years across the three trials, ARTISTIC found no evidence that event-free survival was improved with post-operative radiotherapy compared to early salvage radiotherapy, and 88% of patients reported as event-free.
- Only 39% of men randomised to receive early salvage radiotherapy had required radiotherapy by the time of analysis.
- An early salvage radiotherapy policy means most men can safely avoid adjuvant radiotherapy, reducing side-effects and treatment costs.

## RADICALS-RT

This is the RADICALS-RT part of the RADICALS trial for treating clinically localised prostate cancer. It was designed to compare the efficacy and safety of adjuvant radiotherapy after radical prostatectomy versus a policy of observation with salvage radiotherapy for PSA failure, with a focus on long-term outcome measures. Recruitment to RADICALS took place in hospitals throughout the UK, Canada, Denmark and Ireland, and randomised 1396 patients between October 2007 and December 2016.

## ARTISTIC meta-analysis

ARTISTIC is a prospective systematic review and meta-analysis comparing adjuvant radiotherapy to salvage radiotherapy. It includes data from three trials (including RADICALS), with a total of 2,153 participants with clinically localised disease and median follow-up of five or more years.

### How does adjuvant radiotherapy compare to salvage radiotherapy?

#### Did patients in the salvage radiotherapy arms need radiotherapy?

In RADICALS-RT, one third of those randomised to early salvage treatment had received radiotherapy after a median follow up of five years. This was similar across all the trials in ARTISTIC, which found that, after a median of five to six and a half years of follow-up, only 39% of men randomised to the salvage radiotherapy arms had received radiotherapy.

#### Did adjuvant radiotherapy improve event-free survival?

RADICALS-RT and ARTISTIC looked at whether adjuvant radiotherapy improved the outcome of event free survival. This was defined as the time from randomisation until the first disease event (eg metastases, or a PSA level of at least 2ng/ml). Neither RADICALS-RT nor ARTISTIC found evidence of a difference in event-free survival between the adjuvant and salvage radiotherapy arms at five years. Only 13% of men across the three trials in ARTISTIC had experienced an event by five years. Nearly all events were raised PSA (2ng/ml or high) after radiotherapy had been given (or previously had been indicated for use).

## Further information

Parker C, Clarke N, Cook A et al. 2020. [Timing of Radiotherapy \(RT\) After Radical Prostatectomy \(RP\): First Results from RADICALS-RT Randomised Controlled Trial](#) [NCT00541047]. The Lancet.

## Did adjuvant radiotherapy increase side-effects compared to salvage radiotherapy?

RADICALS-RT found that severe side-effects were generally uncommon. As two thirds of men in the salvage radiotherapy group did not receive radiotherapy, men in this group were less likely to experience the side-effects associated with radiotherapy. Men in the adjuvant radiotherapy group were more likely to report urinary incontinence at one year than men in the salvage radiotherapy group (5% vs 3%). Grade 3-4 urinary strictures within two years were also more common in the adjuvant radiotherapy group than the salvage radiotherapy group (6% vs 4%).

## Did any subgroups of patients benefit from adjuvant radiotherapy?

ARTISTIC found no good evidence that the effect of adjuvant radiotherapy on event-free survival varied according to:

- pre-surgical PSA
- Gleason sum score
- seminal vesicle involvement
- surgical margins
- Risk of prostate cancer recurrence after first-line surgery (CAPRA\_S) risk group

## What do these results mean for clinical practice?

These findings strengthen the case for observation with early salvage radiotherapy only if indicated, after radical prostatectomy. Most men following such a policy will avoid the need for radiotherapy, at least within 5 years after surgery. This will reduce the burden on patients and on the health system.

## Recommendation

Observation with salvage treatment for PSA failure should be the current standard of care after radical prostatectomy.

## Acknowledgements

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Vale C, Fisher D, Kneebone A et al. [Adjuvant or early salvage radiotherapy for the treatment of localised and locally advanced prostate cancer: a prospectively planned systematic review and meta-analysis of aggregate data](#). The Lancet.